

REMARKS

Applicant respectfully requests reconsideration. Claims 1-20, 22, 27-32, 43, 45-57, 63-65, 70-73, 76-80, 83, 84, 88, 89, 94, 95, 97 and 98 were previously pending in this application with claims 10-15, 29, 32, 45-57, 63-65, 70-73, 76-80, 83, 84, 88, 89, 94, 95, 97 and 98 withdrawn. By this amendment, no claims are cancelled or amended. Claims 1-9, 16-20, 22, 27, 28, 30, 31 and 43 are currently under examination with claim 1 being an independent claim. No new matter has been added.

Rejections under 35 U.S.C. § 103(a)

The rejection of claims 1-9, 16-20, 22, 27-28, 30-31 and 43 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Krieg *et al.* (WO 2001/22972) has been maintained.

In the Office Action response filed on January 16, 2008, Applicant presented case law to support the assertion that in the context of an obviousness rejection, a reason must exist for one of ordinary skill in the art to choose a specific compound as a lead compound when presented with several other compounds. Takeda Chemical Industries, Ltd et al. v. Alphapharm Pty., Ltd et al., Case No. 06-1329 (Fed. Cir. June 28, 2007); Eli Lilly and Company and Lilly Industries Limited v. Zenith Goldline Pharmaceuticals, Inc. et al., Case Nos. 05-1396, -1429, -1430 (Fed. Cir. Dec. 26, 2006).

In response to this assertion, the Examiner contends that a rationale does not have to be provided for selecting a single molecule from the prior art because “KSR forecloses the argument that specific teaching, suggestion, or motivation is required to support a finding of obviousness.” KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007). Applicant respectfully disagrees. While the holding in KSR discourages the use of a rigid TSM test for obviousness, it does not preclude the need for a rationale behind the selection of prior art elements for use in a rejection based on obviousness. In KSR, the court held that in a situation where there is a “finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp”. KSR at 1742. However, the determination of what constitutes a “finite number of identified, predictable solutions” depends on the context and the technology. In post-KSR decision Ortho-McNeil Pharmaceutical, Inc., v. Mylan Laboratories, Inc., Case No. 07-1223 (Fed. Cir. March 31, 2008),

the court interpreted the ruling in KSR by stating that “KSR posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness”. Applicant asserts that choosing one single molecule out of over 1000 sequences provided in Krieg *et al.* and then choosing one single nucleotide substitution in the single molecule, did not represent a “small, or easily traversed number of options” in the context of the art. Furthermore, the single molecule that the Examiner has chosen from the art was not highlighted by the art as being a preferred molecule. Applicant reiterates that the Office has not provided a rationale for selecting SEQ ID NO:888 out of all of the oligonucleotides described in Krieg *et al.*

The Examiner contends that one of ordinary skill in the art would have considered it obvious to choose SEQ ID NO:888 of Krieg *et al.* and modify it by one nucleotide to achieve the instant SEQ ID NO:1 based on the assertion that Krieg *et al.* discloses substituting a thymidine for an adenine in a nucleotide sequence to increase its immunostimulatory capacity. The Examiner has not however provided a teaching in Krieg *et al.* to support this position. Rather, the Examiner specifically refers to page 26 lines 2-5 of Krieg *et al.* which states “if the T content of the ODN is reduced by incorporating other bases such as G, A, or C, then the immune stimulatory effects are reduced.” This statement may suggest to one of ordinary skill in the art that, when starting with specific oligonucleotides that have multiple Ts, substituting these T bases with other bases may reduce the immunostimulatory properties of the oligonucleotides. However, one of ordinary skill in the art would not definitively conclude from this disclosure that substituting any given G, A, or C with a T in any oligonucleotide would necessarily increase immunostimulatory capacity of the oligonucleotide. The Examiner has not adequately evidenced a teaching that replacement of any G, A, or C with a T in any oligonucleotide will necessarily increase immunostimulatory capacity.

For the record, in the previous Office Action response, filed on January 16, 2008, Applicant also emphasized that the instant invention was based at least in part on unexpected results. In response, the Examiner states that “[a]pplicant’s specification contains 3 Examples, none of which is directed at comparing Applicant’s SEQ ID NO:1 to SEQ ID NO:246 of Krieg *et al.*” Applicant respectfully disagrees and offers the following clarification. In the Examples section of the instant application, 10104 ODN corresponds to SEQ ID NO:1, and CpG 7909

corresponds to SEQ ID NO:2 and is identical to SEQ ID NO:246 of Krieg *et al.* As a result, the Examples section of the instant application presents a direct comparison of the activity profile between the claimed SEQ ID NO:1 and SEQ ID NO:246 of Krieg *et al.* The results presented in the Examples section indicate that CpG 10104 was found to be as good as CpG 7909 in “augmenting humoral responses against HBsAg in BALB/c mice” and in “promoting Th1 biased immune response” (page 93 lines 19-31; Figures 15 and 16). Clearly, Krieg himself did not know and could not predict which sequence would have an activity profile approximating or exceeding that of SEQ ID NO:246, otherwise this sequence would presumably have been contained in the disclosure of Krieg *et al.*

Reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant respectfully requests reconsideration. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825, under Docket No. C1037.70043US00.

Respectfully submitted,



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